DECLARATION OF JAY NADEL UNDER 37 C.F.R. § 1.132 Address to: Commissioner for Patents Alexandria, VA 22313-1450	Attorney Docket Confirmation No.	UCSF-085 CON5 9049
	First Named Inventor	Jay A. Nadel
	Application Number	10/816,159
	Filing Date	March 31, 2004
	Group Art Unit	1635
	Examiner Name	J.J. Zara
	Title	*Preventing airway mucus production by administration of EGF-R antagonists*

Dear Sir:

1. I, Jay Nadel, declare and say I am a co-inventor of the claims of the above-identified patent application.

2. I have read the Office Action dated March 6, 2007 in this application and understand that the Examiner has rejected pending claims 26-36.

3. The data presented below show that a selective epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor reduces mucin induction in human nasal polyp epithelial cells. Therefore, an EGFR antagonist can be used to treat nasal polyps.

4. We previously showed that human nasal polyp epithelium overexpresses mucins and EGFR. These data were included in Example 8 of the instant application.

5. There is currently no adequate non-human animal model of nasal polyps. Therefore, nasal polyps were obtained from human patients at the time of surgery; epithelial cells were isolated from the nasal polyps, and were cultured *in vitro*. The cells were grown to confluence and were serum-starved for 8 hours.

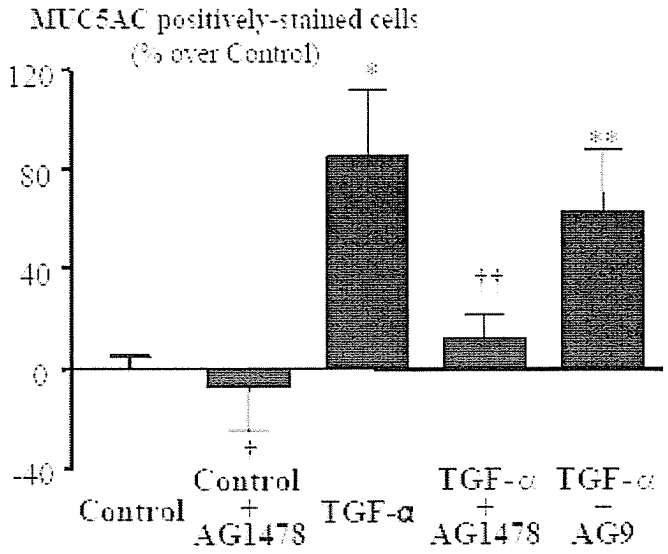
6. The cultured nasal polyp epithelial cells were then treated with transforming growth factor-α (TGF-α), a cytokine known to induce EGFR expression in human airway epithelium. For inhibition studies, the cells were pre-treated with AG1478, a selective EGFR tyrosine kinase inhibitor, or with a negative control compound, AG9.

7. After culturing the cells for 24 hours, immunocytochemical staining for mucin (MUC5AC) protein was performed, and the number of positive cells was counted. TGF-α treatment increased the number of mucin-staining cells. These results were confirmed by measurement of mucins by enzyme-linked immunosorbent assay.

8. Pretreatment of the cultured nasal polyp epithelial cells with AG1478 strongly inhibited TGF-α-induced mucin production, as shown in Figure 1A and Figure 1B. The control compound AG9 did not inhibit TGF-α-induced mucin production.

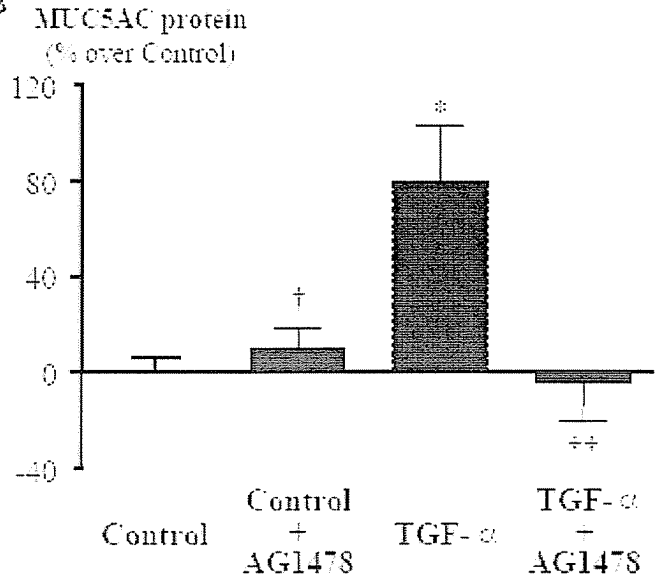
9. The data shown in Figures 1A and 1B show that a selective EGFR tyrosine kinase inhibitor reduces mucin production in human nasal polyp epithelial cells. The data indicate that selective EGFR tyrosine kinase inhibitors can be effective in treating nasal polyps.

Figure 1A



*. $P < 0.01$; **. $P < 0.05$ compared to Control
+. $P < 0.05$; + +. $P < 0.05$ compared to TGF-α
n = 4 independent experiment in duplicate

Figure 1B



*. $P < 0.05$ compared to Control

†. $P < 0.05$; ††. $P < 0.05$ Compared to TGF-α

n = 3 independent experiments in duplicate

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

7/26/07
Date

Jay Nadel
Jay Nadel

F:\DOCUMENT\UCSF\085con5\Decl Rule 132.doc